Preliminary Amendment to supplement provisionally elected Group II. Applicants also provide herein a revised Sequence Listing.

Restriction Requirement

Although applicants provisionally elect Group II (claim 26) with traverse, applicants request that the restriction requirement be reconsidered because the Examiner has not shown that a serious burden would be required to examine all the claims. M.P.E.P § 803 provides:

> If the search and examination of an application can be made without serious burden, the Examiner **must** examine it on the merits, even though it includes claims to distinct or independent inventions.

M.P.E.P § 803 (emphasis added). Thus, for a restriction to be proper, the Examiner must satisfy the following two criteria: (1) the existence of independent and distinct inventions (35 U.S.C. § 121); and (2) that the search and examination of the entire application cannot be made without serious burden. *See* M.P.E.P § 803.

The Examiner has not shown that the **second** requirement has been met. Specifically, the Examiner has not shown that it would be a serious burden to search and examine all of the groups together. Specifically, Group II and III should be combined, because Group III is a method of using the immunotoxin of Group II, and it would not be a serious burden to search and examine a method of using the immunotoxin simultaneously with a search of the immunotoxin itself. If claims to the immunotoxin are patentable, then claims to a method of using the

immunotoxin are also patentable. Furthermore, the absence of a serious burden in searching and examining Groups II and III is particularly true because claim 26 has been amended herein to claim one immunotoxin construct from the original group of eight in original claim 26, thereby minimizing the Examiner's search and examination for Group II. Consequently, reconsideration and modification or withdrawal of the restriction is requested. Applicants furthermore remind the Examiner that upon allowance of the claims of Group II, the claims of Group III will be allowable under Rejoinder Practice as provided in M.P.E.P. § 821.04.

Preliminary Amendment

Claim 26 is amended to claim an anti-T cell immunotoxin fusion protein comprising a diphtheria toxin moiety and a targeting moiety, wherein the sequence from the amino terminus from left to right is toxin moiety,VL,L,VH,L,VL,L,VH, and wherein the toxin moiety comprises a truncation mutation, L is a (G4S)3 linker, VL and VH are the variable light and heavy domains of the anti-CD3 antibody UCHT1, and H is the γIgG hinge. Support for this amendment can be found in claims 8, 24, and 26, as originally filed. Claim 26 has been further amended to recite a SEQ ID NO for the (G4S)3 linker, which is provided as SEQ ID NO:16 in the revised sequence listing.

Claim 27 has been amended to depend on claim 26. Support for this amendment can be found in claims 26 and 27 as originally filed. New claim 43 is inserted herein by amendment.

Claim 43 provides the immunotoxin fusion protein, wherein the truncated diphtheria toxin comprises 390 residues from the N-terminal glycine of mature diphtheria toxin. Support for this amendment can be found in claims 23 and 24 as originally filed and throughout the specification. No new matter is believed to be added by these amendments, and entry of the amendments and consideration of the claims are requested. A copy of marked-up versions of the amended paragraphs of the specification and the amended claims is provided as Attachment A.

With respect to the claim added with the Preliminary Amendment herein, applicants respectfully request that new claim 43 be properly grouped with Group II. Applicants therefore respectfully await an action on the merits.

Sequence Listing

The Examiner stated that the sequence in claims 9 and 10 must be brought into compliance with 37 C.F.R. §§ 1.821-1.825. Claims 9 and 10, however, are withdrawn from consideration without prejudice and the objection is believed to be moot. Nonetheless, counsel for applicants provide herein a revised Sequence Listing in the form of paper sheets and a computer readable diskette to comply with 37 C.F.R. § 1.821 - 1.825 with regard to the sequence provided in claim 26. A new sequence in the form of SEQ ID NO:16 is included. Support for this sequence can be found in claim 26 as originally filed and on page 22, line 1. The material on the diskette and that in the hard copy of the Sequence Listing are the same and contain no new

matter. Entry of the revised Sequence Listing is respectfully requested.

A check in the amount of $128.00 is enclosed for the additional claim submitted with the Preliminary Amendment ($18.00) and a one-month Request for Extension of Time ($110.00) herewith. No other fees are believed due; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No.14-0629.

Respectfully submitted,

Tina Williams McKeon
Registration No. 43,791

NEEDLE & ROSENBERG, P.C.
Suite 1200, The Candler Building
127 Peachtree Street, N.E.
Atlanta, Georgia 30303-1811
(404) 688-0770

I hereby certify that this PRELIMINARY AMENDMENT AND RESPONSE TO RESTRICTION REQUIREMENT is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner of Patents, Washington, D.C. 20231, on the date shown below.

Tina Williams McKeon

March 13, 2001
Date

Attachment A
Marked-up Version of Amended Paragraphs and Amended Claims

Amended Paragraphs of Specification

Page 22, lines 1-3:

Tox,μCH2,μCH3,VL,L,VH where L is a (G4S)3 (SEQ ID NO:16) linker and VL and VH are the variable light and heavy domains of the anti-CD3 antibody UCHT1.

Amended Claims

26. (Amended) An [The divalent] anti-T cell immunotoxin [of claim 24, wherein the immunotoxin is a] fusion protein comprising a diphtheria toxin moiety and a targeting moiety, wherein [and] the sequence [of domains] from the amino terminus from left to right is [selected from the group consisting of:

toxin moiety,μCH2,μCH3,VL,L,VH;
toxin moiety,μCH2,μCH3,μCH4,VL,L,VH;
toxin moiety,γCH3,H,VL,L,VH;
toxin moiety, H,VL,L,VH; and
toxin moiety,μCH2,VL,L,VH
toxin moiety,VL,L,VH,H,γCH3
toxin moiety,VL,L,VH,μCH2]
toxin moiety,VL,L,VH,L,VL,L,VH,

wherein the toxin moiety comprises a truncation mutation, L is a (G4S)3 (SEQ ID NO: 16) linker, VL and VH are the variable light and heavy domains of the anti-CD3 antibody UCHT1, and H is the γIgG hinge.

27. (Amended) A method of inhibiting a rejection response by inducing immune tolerance in a recipient to foreign mammalian donor cells, comprising the steps of:

a) exposing the recipient to [an]the immunotoxin of claim 26 so as to safely reduce the recipients's T-cell lymphocyte population by at least 80%; and
b) transplanting the donor cells into the recipient, such that a rejection response by the recipient to the donor organ cell is inhibited.

43. (New) The immunotoxin fusion protein of claim 26, wherein the truncated diphtheria toxin comprises 390 residues from the N-terminal glycine of mature diphtheria toxin.